ATTACHMENT A

PATENT
Customer No. 22,852
Attorney Docket No. 07588.0082

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	
David Dakin Iorwerth WRIGHT et al.	Group Art Unit: 1616
Application No.: 10/522,527	Examiner: Soroush, Ali
Filed: October 10, 2006	
For: THERAPEUTIC FOAM	Confirmation No.: 7497

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

DECLARATION UNDER 37 C.F.R. § 1.132

I, David WRIGHT, do hereby make the following declaration:

1. I am one of the inventors of U.S. Patent Application No. 10/522,527, filed October 10, 2006.

2. I have been awarded a BSc (Hons) in medical physics, and I am an MB and BS (UK doctor and surgeon) and a fellow of the Royal College of Surgeons.

3. I am Vice President of Medical Affairs at BTG. During my employment at BTG, I have been engaged in research and development in the treatment of varicose veins.

4. Injection of gas and sclerosant based foams are widely used to treat varicose veins without surgery. In patients with a patent foramen ovale (PFO), i.e., a hole in the heart, intra-arterial gas embolism is a potential concern because gas bubbles

can cross (through the PFO or other right to left vascular shunt) from the venous to the general arterial circulation, and distributed to all organs including the brain and eye, where they can cause neurological symptoms and visual disturbances .

5. I am familiar with a study by Eckmann et al (Dermatol. Surg. June 2005; 31(6): 636-43) which looked at gas bubble dimensions and dynamics of different foam formulations injected into the cremaster arterial microcirculation of the rat.

6. The study compared the following formulations of polidocanol foam:

(1) an air based foam,

(2) the "old" microfoam containing 7% nitrogen (referred to in the Eckmann study as "Varisolve® Type A"), and

(3) the "new" microfoam containing 0.01-0.8% nitrogen (referred to in the Eckmann study as "Varisolve® Type B").

7. Each formulation was injected into the femoral artery of a rat and small cremaster vessels (10-200 µm in diameter) were viewed using videomicroscopy to observe the size and number of gas bubbles as well as their behavior (e.g., lodging and clearance in the arterioles). The authors observed distinct differences among foam formulations for both the number and size of circulating bubbles.

8. The study surprisingly demonstrated that injection of the old Varisolve® foam (7% nitrogen) resulted in visible bubbles in rat cremaster vessels, while injection of the new Varisolve® foam (0.01-0.8% nitrogen) resulted in virtually no bubbles.

9. Specifically, a total of twenty-seven bubbles were observed after injection of the Varisolve® type A foam (7% nitrogen) in the 6 rats tested (in one trial no bubbles were observed). In contrast, in 5 of the 6 trials with the Varisolve® type B foam (0.01-

0.8% nitrogen) no bubbles were observed. In the sixth trial, only two bubbles were observed.

10. Injection of the air based foam resulted in large bubbles (mean bubble volume of 2.72 nL) which lodged within the rat arterioles, obstructing blood flow, at the smallest dose tested, while injection of the Varisolve® Type A and B microfoams resulted in smaller bubbles (mean bubble volume of 0.53 nL and 0.20 nL, respectively), which did not obstruct arterioles even at the largest dose tested (eight times the smallest). In fact, the bubbles observed after injection of the Varisolve® Type B foam (0.01-0.8% nitrogen) were only visible with image enhancement.

11. Attachment B includes microscopic images of the rat vessels, showing the bubbles produced by injection of each type of foam. The image of the air based foam shows multiple bubbles lodged in the arterioles, blocking blood flow. In comparison, the image of the Varisolve® type A foam (7% nitrogen) shows transiting (i.e., not lodged) bubbles of smaller size than the air foam but still greater than the diameter of the arterioles while the image of the Varisolve® type B foam (0.01-0.8% nitrogen) shows transiting bubbles of with much smaller dimensions, bubble diameters a fraction of vessel width.

12. Previously, practitioners believed that injection of a foam containing 7% nitrogen carried an acceptable risk of intra-arterial gas embolism and, therefore, practitioners did not believe that lowering the amount of nitrogen gas was necessary nor would it result in sufficient gains in safety to justify the added difficulty and expense of producing a foam with a nitrogen content of 0.01-0.8%. However, the Eckmann study

surprisingly demonstrated that the new Varisolve® type B foam (0.01-0.8% nitrogen) displayed distinct differences from the Varisolve® type A foam (7% nitrogen).

13. In my opinion, these differences (i.e., fewer, smaller bubbles) render the Varisolve® type B foam (0.01-0.8% nitrogen) safer (i.e., lower risk of intra-arterial gas embolism) than the Varisolve® type A foam (7% nitrogen).

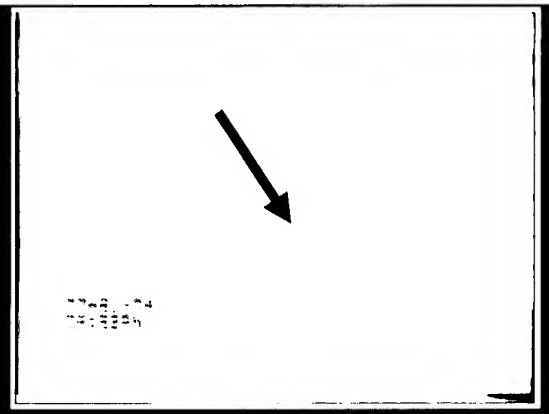
14. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Dated: November 24th, 2008

By: _____
Dr. David Wright

Intravital Microscopy of Microfoam Injected into Rat Cremaster Microvasculature

Attachment B



Air-Based Polidocanol Foam (Tessari Method)

Still photo of air-based foam bubbles lodged in arterioles; no change over 30 minutes

"OLD" **Microfoam 7% nitrogen**

Video-frame capture of proprietary microbubbles which were much smaller and did not obstruct arterioles

"NEW" **Microfoam 0.01-0.8% nitrogen**

Video-frame capture of bubbles only visible with image enhancement; did not obstruct arterioles

Eckmann DM (2005) Derm Surg; 31:636-643.

Attachment C